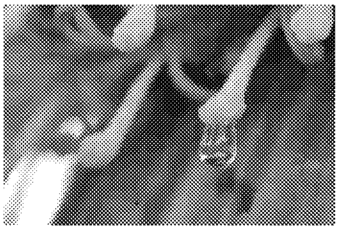

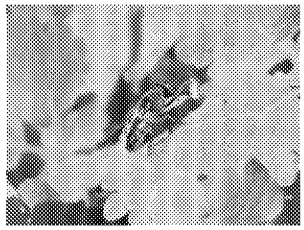

Neonic Risk Assessments – Final Bee, Aquatics, & Terrestrial

(Clothianidin, Dinotefuran, Imidacloprid, and Thiamethoxam)

Briefing for OPP OD

August 28, 2019

Final Bee Risk Assessment
Methods

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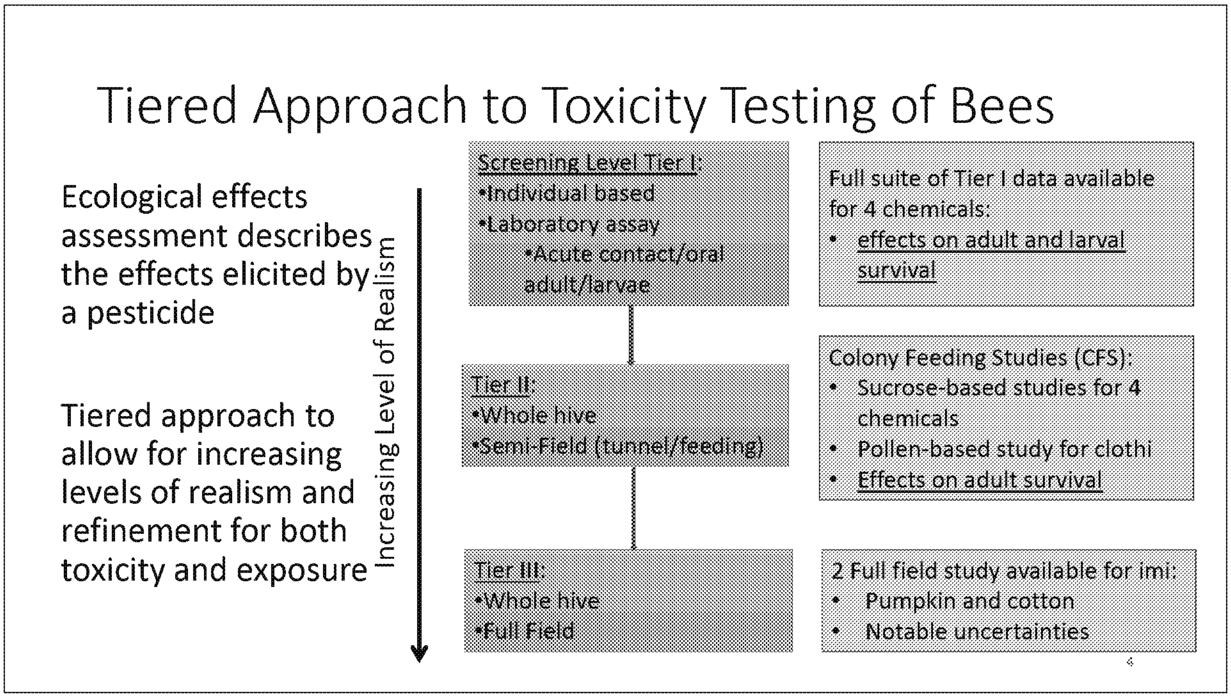
Moving into the final bee risk assessment methods…

Protection Goals and Assessment Endpoints

Protection Goal	Assessment Endpoints	Measurement Endpoints (Population level and higher)	Measurement Endpoints (Individual Level)
1. Provision of Pollination Services	Population size and stability of managed bees	Colony strength and survival	Individual worker survival Queen fecundity Brood size Worker bee longevity
2. Production of Hive Products	Quantity and quality of hive products	Quantity and quality of hive products	Individual worker survival Queen fecundity Brood success
3. Contribution to Pollinator Biodiversity	Species richness and abundance	Colony strength and survival Species richness and abundance	Individual worker survival Brood success

Protection goals have been developed for the colony level with measurement endpoints at both the colony and individual level. I'll note that we largely focused on honey bees for the neonic assessments based on the needs of PRD; however, the assessments also considered non-honey bee species in qualitative manner.



Risk to bees is assessed with a tiered approach that is designed to allow for increasing levels of realism and refinement for both toxicity and exposure as you move up the tiers. I'll note that before we even start with tier 1, we consider potential for exposure using USDA bee attractive guidance. Those crops that are not pollinator attractive are still evaluated for potential off-field effects (e.g., from spray drift). For pollinator attractive crops, the screening level, or Tier 1, is based on lab studies at the individual bee level. For the neonics, lab data are available for acute contact and acute/chronic oral studies for adults and larvae from both registrant submissions and open literature. Tier 2 evaluates the whole hive with semi-field tunnel/feeding studies. For the neonics, colony feeding studies conducted with sucrose are available for all 4 chemicals, while a pilot colony feeding study conducted with pollen is available for clothianidin. And finally, Tier 3 evaluates the whole hive with a full field study. For the neonics, there are two full field studies available for imidacloprid (one for pumpkin and one for cotton, though both studies had notable uncertainties that limited their utility in risk assessment).

In addition to the available toxicity data, a large database of pollen and nectar residue data is available across the four neonics. This residue data is used in both the Tier 1 and Tier 2 risk assessment.

Tiered Approach for Bee Assessments

- Tier 1 analysis
  - BeeREX for on-field default and refined exposures
  - AgDrift for off-field exposures

- Tier 2 analysis
  - Nectar equivalents method to combine residues in pollen and nectar (replaces "bee bread" method)
  - Residue bridging strategy to evaluate magnitude and duration of exposures
  - Strength of evidence based on evaluation of multiple lines of evidence

On the exposure side, at the Tier 1 we use BeeREX for on-field exposures. Default estimates of exposure are refined using the available chemical-specific residue data. Also at the Tier 1, we use AgDrift to evaluate potential off-field exposures. As a result of the new colony feeding studies and large residue database, we developed a new Tier II method for estimating colony-level exposures. We'll go into details in the next few slides, but at the high level, the new approach combines pollen and nectar residue in a way that is responsive to public comments, more biologically relevant, and consistent with the approach used at Tier I. This approach replaces the previous "bee bread" method. We also developed a residue bridging strategy that allows us to make the best use of the available residue data to 1) distinguish between green and red calls with some level of confidence, and 2) gives us the ability to inform on potential mitigation options, e.g., a pre-bloom interval that would preclude potential risk. And, as stated previously, we included the non-ag use sites as part of the risk assessment.

New Tier 2 Exposure Methodology –Pollen + Nectar (Replaces "bee bread" method)

- Honey bee colonies consume more nectar than pollen
  - If concentrations in pollen and nectar are equal, dose from nectar will be greater
- Available information suggest that on a concentration basis, colony level endpoints for nectar should be lower than pollen
- Route of exposure does not appear to influence toxicity
- Three lines of evidence indicate that difference in contribution of colony's dose from pollen is 20x less than that of nectar
- Final equation:

$$\boxed{C_{total} = C_{nectar} + \frac{C_{pollen}}{20}}$$

We'll start with the nectar equivalents method. The Tier II pollen and nectar method is a way of combining measured concentrations for both matrices into a concentration in total diet that essentially converts residues in pollen to nectar equivalents by the application of a 20x factor. This factor was determined by evaluating three separate lines of evidence that all sort of converged. These are presented on the slide here and include: an evaluation of consumption rates and a comparison of tox endpoints on a concentration and dose basis.

The final equation used to estimate a total dietary concentration at the bottom was used in the risk assessments.

New Tier 1 and 2 Exposure Methodology – Residue Bridging Strategy

- Using ~80 neonic residue studies, EFED developed methods to reduce uncertainties in existing neonic residue database for assessing risk to bees due to:
  - **Lack of data** (missing chemical/crop/method)
  - **Data limitations** (sparse temporal, spatial coverage, missing matrix)
- Improve how residue data are applied to bee risk assessment
  - Harmonize methodology with other taxa (birds/mammals), EFSA
- Address residue data for applicable non-agricultural uses
- Residue bridging strategy documents that explain the methodology in detail will be provided as Attachments to the Final Bee RAs (1 – soil and foliar applications; 2 – seed treatment applications; 3 – non-ag applications)

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Moving on to the residues, the goals of the bridging strategy were to 1) develop methods to reduce uncertainties in the existing database due to lack of data or various data limitations; 2) improve how residues are applied to bee risk assessments by attempting to harmonize the methodology, where sufficient data were available, with those employed for other taxa or by other regulatory bodies; 3) and finally, to develop an approach for non-ag uses.

Distinct approaches were developed for seed treatments vs foliar/soil applications.

New Tier 2 Exposure Methodology – Residue Bridging Strategy

- Extremely broad neonicotinoid use pattern necessitated extrapolation of bee-relevant residue data to address gaps and limitations in data
- Relied on a data-driven bridging strategy from over 80 bee-relevant residue studies to extrapolate residues, when necessary, across:
  - Chemicals, application rates, crops, matrices, time, sites
- Improved consistency in how residue data are applied to bee risk assessment
- Incorporated residue data for non-agricultural uses
- Detailed residue bridging strategy documents provided as Attachments to the Final Bee RAs
  - 1 – soil and foliar applications; 2 – seed treatment applications; 3 – non-ag applications

Moving on to the residues, the goals of the bridging strategy were to 1) develop methods to reduce uncertainties in the existing database due to lack of data or various data limitations; 2) improve how residues are applied to bee risk assessments by attempting to harmonize the methodology, where sufficient data were available, with those employed for other taxa or by other regulatory bodies; 3) and finally, to develop an approach for non-ag uses.

Distinct approaches were developed for seed treatments vs foliar/soil applications.

Residue Bridging Strategy

- Determined the major, quantifiable variables that influence residue levels
  - Application method, application timing, and site
  - Chemical was not an influential variable for most crops
  - Crop does sometimes influence concentrations
    - limits bridging outside of crop groups
- Developed approach for incorporating residue data into risk assessment
  - Derive Tier 1 (refined) and Tier 2 exposure concentrations
  - For those uses with sufficient data to quantify kinetics of residue declines (*i.e.,* foliar applications for cotton, cucurbit, and berries), Monte Carlo analyses were utilized
    - Probabilistic approach to predict residue concentrations
    - Allowed for calculation of the number of days required for residues to drop below the toxicity endpoint.
    - For orchards (pre-bloom, foliar), data were combined from available studies to derive median estimated values over time

The residue bridging analyses identified application method, application timing, and site as the major, quantifiable variables that influence residue levels. I'll note that there are nuances to this and that while these variable consistently came up across the crops/crop groups, others were also identified on a case by case basis. We considered these influential variables in the weight of evidence when making risk calls. Through this process we also developed an approach for how to incorporate the residue data into the risk assessment. At a minimum, the colony level endpoints are compared to the residue data for each crop/crop group adjusted to the appropriate maximum application rate. Then, if there is sufficient data to quantify the kinetics of residue declines, a Monte Carlo analysis was conducted to predict a distribution of daily residue concentrations. This was only possible for foliar applications to cotton, cucurbits, and berries. This allowed for the calculation of the number of days required for residues to drop below the colony level endpoint. For foliar pre-bloom applications to orchards a slightly different approach was taken. In this case the residue data was not sufficient for use in the Monte Carlo analysis, but it was determined that it was possible to combine all of the available data to derive median estimated values over time. Either way, this was useful for risk mitigation purposes (e.g., pre bloom restriction windows).

General Trends Observed in Residue Data

- Residues from foliar applications > soil applications > seed treatments
  - Residues from foliar applications = 100 - 1000s ppb
  - Residues from soil applications = 10 - 100s ppb
  - Residues from seed treatments = 1 - 10s ppb
- Faster decline after foliar application vs. soil application
- ~~Although residues from foliar applications are generally higher in magnitude, they decline more rapidly than soil applications (which tend to persist in pollen and nectar for much longer time periods)~~
- Pre-bloom applications result in residues that are generally much higher than post-bloom applications

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Based on these analyses we saw some general trends in the data. At the 30,000 foot level, residues from foliar applications are greater than residues from soil applications, which are greater than residues from seed treatments. [Ranges presented here represent the max values normalized to 0.1 lb/a for foliar and soil applications and 1 mg/seed for seed treatments.] SPOILER ALERT: colony feeding study endpoints are in the 10s for IMI, CLOTHI, and THIA and 100-ish for DINO. I'll note that the range of residues presented for foliar applications is based on samples taken close to application (~2 weeks). After that the second bullet comes into play because residues from foliar applications tend to decline much more rapidly than residues from soil applications, with a steeper slope. Generally there is also a distinction between pre-bloom and post-bloom applications, with the former being greater.

Based on these general trends we decided to separated foliar and soil applications as well as pre-bloom and post-bloom applications. You'll see how this factors into the risk calls in a few slides.

Residue Bridging Strategy Conclusions

- For use sites with sufficient data, residues are bridged across chemicals, including:
  - Cotton: foliar, seed treatment
  - Cucurbits: foliar, soil, seed treatment
  - Orchards (Stone fruit, pome fruit, citrus, tree nuts, tropical fruit): foliar, soil
  - Berries and small fruits: foliar, soil
  - Fruiting vegetables (*e.g.*, peppers): foliar, soil
  - Soybeans: foliar, soil, seed treatment
  - Canola: seed treatment
  - Ornamentals: foliar, soil
  - Turf: foliar
- For use sites with insufficient data, residues from other crops are used as surrogates

The bottom line for the residue bridging strategy is that we maximized The robustness of the available residue data is considered as part of the strength of evidence

Lines of Evidence Considered in Making Risk Calls

- Bee Attractiveness
- Agronomic practices (*e.g.,* harvest time relative to bloom)
- Residues above Tier 2 NOAEC and LOAEC
  - Chemical / crop specific residue data
  - Bridging strategy residue data (from other crops or across chemicals)
  - Duration and frequency of LOC exceedance
  - Magnitude of exceedance
    - Ratio of max residue value to NOAEC/LOAEC
    - % of diet from the treated field needed to reach the NOAEC/LOAEC
  - Geographical scale and spatial distribution of crop group / use pattern; usage
- Incidents

Several lines of evidence were considered in making risk calls. At Tier I, we considered whether the crop was honey bee attractive, as well as any agronomic practices that may limit exposure, e.g., harvest time or flower tenting (as in the case of mandarin oranges). At Tier I we also considered whether predicted or measured residues exceed the individual effect level endpoints, which they mostly did. At the Tier II we considered whether residues exceeded the colony level endpoints. This was the major basis for a risk call; however, we provided several additional pieces of information to better characterize the potential for risk, including whether the exceedances were based on chemical specific or bridged residue data; the duration, frequency, and magnitude of the exceedance; and the geographic scale and spatial distribution of the use. And then there are the incidents. The teams incorporated this additional characterization into a discussion of the strength of the risk call for each crop/crop group within a chemical.

Add discussion of persistence, systematicity, of chemical class and why we care about duration and frequency.

Strength of Evidence

- Strong Evidence of Risk
  - Residues exceed colony-level endpoint(s) by a high magnitude, frequency, and/or duration
  - Chemical-specific or robust bridged residue data set available
  - Residues exceed across multiple locations
  - May be supported by modeled (*e.g.*, Monte Carlo) exposures or ecological incidents

- Moderate Evidence of Risk
  - Residues exceed colony-level endpoint(s) but magnitude, frequency, and/or duration are limited
  - Residues exceed across few locations
  - Maybe supported by limited ecological incident information

- Weak Evidence of Risk
  - Residues exceed colony-level endpoint(s) but there are uncertainties in the surrogacy in the bridged residue data set
  - Majority of residues below toxicity endpoint
  - Residues exceed at one location
  - Not supported by ecological incidents

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As part of the strength of evidence, we considered how the major assumptions of our assessment approach influence the risk call (e.g., 100% of the colony's diet comes from the treated field, a single exposure is enough to trigger the effect observed in the CFS). For a crop group with strong evidence of risk, maybe only 1% of the colony's diet would need to come from a treated field, measured and modeled residues across multiple geographic locations are above the colony level endpoint for several weeks, and these conclusions are supported by a robust set of chemical-specific or bridged residue data and potentially incidents as well. This suggest that no matter where the chemical is applied in the country, if a hive is in proximity to a treated field there is potential for a chance exposure to cause effects at the colony level. For a crop group with moderate evidence of risk, maybe a larger portion of the colony's diet would need to come from a treated field or residues across a few geographic locations are above the colony level endpoints for less than a week, and while there may be incident information, there is some recognized variability in the potential for exposure. For a crop group with weak evidence of risk, maybe there are uncertainties related to the surrogacy of the bridged residue data, or maybe a majority of the available residues are below the level of concern, suggesting uncertainties in the potential for exposure.

Since this weighing of the evidence is by nature a subjective process, the teams coordinated to ensure consistency in our calls.

Final Bee Risk Assessment
Conclusions & Characterization

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Moving into the risk characterization… the discussion will focus on honey bee risk and will end with some characterization for other species of bees

Low Risk Calls

Foliar and Soil Applications

Crop Group or Crop	IMI		CLOTHI		THIA		DINO	
	Foliar	Soil	Foliar	Soil	Foliar	Soil	Foliar	Soil
Bulb Vegetables								
Leafy Vegetables								
Brassica Vegetables								
Legumes								
Cereal Grains								
Cucurbits								
Citrus Fruits	**	**	Post-	Post-	Post-	Post-		
Pome Fruits			Post-		Post-			
Stone Fruits			Post-		Post-		Post-	Pre-/Post-
Tree Nuts	Post-		Post-		Post-			
Tropical Fruits			Post-		Post-			
Berries/Small Fruits	Post-	Post-	Post-	Post-	Post-	Post-	Post-	Post-
Root/Tubers*								
Fruiting Veg*								

Seed Treatments

Crop Group or Crop	IMI	CLOTHI	THIA
Bulb Vegetables			
Leafy Vegetables			
Brassica Vegetables			
Legumes			
Cereal Grains			
Oilseed			
Cucurbit Vegetables			
Root/Tuber Vegetables*			

* Denotes call is for non-attractive crops
** Mandarin Orange Crop tented during bloom

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This table summarizes the low risk calls for foliar and soil applications, represented by green cells. The gray cells indicate either the chemical is not registered for a particular use or there was a risk call (we'll get to those soon). For orchards and berries and small fruits, risk calls are distinguished for pre-bloom vs. post-bloom applications, which was a recommendation from the residue bridging strategy.

Crops/crop groups were considered low risk because they were harvested prior to bloom (e.g., bulb, leafy and brassica vegetables; artichoke and tobacco), not considered attractive to honey bees (i.e., certain crops within the root and tuber and fruiting vegetables crop groups), or had measured residues below the colony-level effects endpoints. The figure on the right is an example for foliar post-bloom applications to berry and small fruit crops where the residues are substantially lower than the imidacloprid colony level NOAEC and LOAEC.

A few things to note: the calls for root and tubers and fruiting vegetables are for non-attractive crops within the groups, and the call for IMI citrus is only for mandarin oranges, which are tented... all other citrus are high for both foliar and soil applications.

ADVANCE SLIDE: The table on the right summarizes the low risk calls for seed treatments, which accounts for the large majority of usage for imi, clothi, and thia. So things like soybean, corn, which are major uses for these chemicals, were identified as low risk (not accounting for dust-off)

Some of these crops were "uncertain" in the preliminary assessments, but the additional data generated for these 3 chemicals allowed us to make "low risk" calls.

[other green calls for thia include: artichoke, tobacco, peanuts, sod, christmas trees and other outdoor residential (eg crack and crevice)]

Summary of Risk Conclusions for Foliar Applications

Crop Group or Crop	Imidacloprid		Clothianidin		Thiamethoxam		Dinotefuran	
Cotton	Strongest		Strongest		Strongest		Strongest	
Cucurbit Vegetables			Strongest		Strongest		Moderate	
Citrus Fruits	Pre- Strongest	Post- Weakest			Pre- Strongest	Post-		
Pome Fruits	Pre-	Post- Weakest	Pre-	Post-	Pre- Strongest	Post-		
Stone Fruits	Pre-	Post- Weakest	Pre-	Post-	Pre- Strongest	Post-	Pre- Strongest	Post-
Tree Nuts	Pre-	Post	Pre-	Post-	Pre- Strongest	Post-		
Tropical Fruits	Pre- Strongest	Post- Weakest	Pre-	Post-	Pre- Strongest	Post-		
Berries/Small Fruits	Pre- Strongest	Post-	Pre- Strongest	Post-	Pre- Strongest	Post-	Pre- Strongest	Post-
Root/Tubers Vegetables*	Weakest		Weakest		Weakest		Weakest	
Fruiting Vegetables*	Strongest				Strongest		Strongest	
Herbs/Spices	Weakest				Weakest			

The next few tables summarize the risk calls for agricultural crops. This table summarizes the risk conclusions for foliar applications. Red cells are risk, green cells are low risk, and gray cells are not registered. As with the low risk calls, for orchards and berries and small fruits, risk calls are distinguished for pre-bloom vs. post-bloom applications. Note that most of these calls were yellow in the preliminary assessments due to gaps in the residue database. Bridging really allowed us to make them all green or red. This table also identifies the strength of evidence for the risk call in black text. Cotton, cucurbits, pre-bloom orchard, pre-bloom berries and small fruits, and honey bee attractive fruiting vegetables are strongest evidence of risk for all chemicals.

Summary of Risk Conclusions for Soil Applications

Crop Group or Crop	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Cotton	Moderate			
Cucurbit Vegetables	Strongest	Moderate	Moderate	
Citrus Fruits	Pre- Strongest; Post- Moderate	Pre-; Post- Moderate	Pre- Strongest; Post- Weakest	
Pome Fruits	Pre-; Post- Weakest			
Stone Fruits	Pre-; Post- Weakest			Pre- Weakest; Post-
Tree Nuts	Pre-; Post- Moderate			
Tropical Fruits	Pre-; Post- Weakest			
Berries/Small Fruits	Pre- Strongest; Post-	Pre-; Post-	Pre- Strongest; Post-	Pre- Moderate; Post-
Root/Tubers Vegetables*	Weakest	Weakest	Weakest	Weakest
Fruiting Vegetables*	Strongest		Moderate	Weakest
Herbs/Spices	Weakest			

* denotes call is for honeybee attractive crops within the crop group

Here is the table summarizing risk conclusions for soil applications. Where the foliar applications are mostly strong evidence of risk, the soil applications are more moderate and weak evidence. This is because, as you may recall from our previous discussion of the general trends in residue data, residues from soil applications tend to be lower than foliar applications but they may persist for much longer.

Summary of Risk Conclusions for Seed Treatments

Crop Group or Crop	Imidacloprid	Clothianidin	Thiamethoxam
Bulb Vegetables			
Leafy Vegetables			
Brassica Vegetables			
Legumes	Weakest (Beans)		
Cereal Grains			
Oilseed			
Cucurbit Vegetables			
Root/Tubers Vegetables*		Weakest (Turmeric only)	

* denotes call is for honeybee attractive crops within the crop group

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Here is the table summarizing the risk conclusions for seed treatment uses. As you can see, most of the seed treatments are low risk, as we discussed previously, with the couple of exceptions noted here.

Risk Calls – Non-Ag Uses

- Ornamentals and forestry
  - Strongest evidence of risk for ornamentals (all chemicals) and forestry (imi, dino)
  - Incidents for IMI, CLOTHI, and DINO
  - Uncertainty considerations:
    - Very limited data set for a diverse set of plants
      - Unable to refine exceedances based on time
    - Application rates, scaling to lb/A for a standard evaluation is difficult
- Turfgrass (residential): moderate evidence of risk for all chemicals
  - Residues from open literature study with IMI and CLOTHI
  - Based on the assumption of flowering weeds on residential lawns

For non-agricultural ornamentals and forestry uses, residue data are available for IMI (soil), THIA (foliar and soil), and DINO (foliar and trunk injection). While ornamental plants are of known pollinator attractiveness just from everyone observing bees in our gardens, IR-4 has developed a website that contains a list to help gardeners find ornamental plants they can use in their gardens to serve as a resource for foraging pollinators. In addition, various tree species are considered bee attractive, e.g., maple, serviceberry, crapemyrtle, black tupelo, sourwood, black locust, and linden. In addition, an article by Hill and Webster (1995) discusses the potential economic benefits of combining apiculture and forestry operations as many of the commercially valuable trees produce nectar and pollen that are available during the spring, when other bee resources are limited.

The assessment for residential turf assumes that bee attractive weeds are present and flowering during application.

For ornamentals and forestry uses, while there are notable uncertainties, residue levels are in the PPM range. These large exceedances are likely much greater than any chemical specific influence we would see (based on foliar/soil residue).

For residential turf uses, while residues are again in the PPM range, there is uncertainty related to the assumption that flowering weeds are present on residential lawns to serve as a potential exposure route.

Off-site Risk Conclusions

- Spray drift: off-field dietary risks to individual bees extend 1000 feet from the edge of the field
- Clothi and IMI poultry house uses risk based on Tier I
  - Risk call is based on treated poultry litter subsequently applied to an agricultural field
  - No residue data are available
  - Imi – No label specific restrictions for area treated or house treatments before cleanout
  - Clothi - Incorporates proposed mitigation scenarios from the registrant (does not change the risk call, but exposures are considerably reduced under these mitigations)

In addition to the Tier II risk conclusions there are Tier I conclusions that have not changed from the preliminary assessments, including conclusions for the clothi poultry and risks from spray drift presented here.

Based on a Tier I analysis, for foliar applications, off-field dietary risks to individual bees exposed to spray drift extend 1000 feet from the edge of the treated field. There is uncertainty in this conclusion which includes: assumption of available attractive forage off field, use of individual level toxicity data, BeeREX default estimates for residues, and unrefined AgDRIFT™ modeling.

Non-*Apis* Risk Conclusions

- Comparison of tox data and previous analysis of exposure indicate that honeybees are an appropriate surrogate for other bee species (bumblebee, etc.)
  - Red risk calls for honey bees extend to non-Apis species
  - Fruiting vegetable green calls for honey bees are red for non-Apis

Surrogate both at individual and colony level

Fruiting vegetable green calls for honey bees are based on lack of attractiveness, and are red for non-Apis.

Aquatic and Terrestrial Taxa (non-bee) Risk Conclusions

& New Data Analysis

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Moving into the risk characterization…

Terrestrial Big Picture Risk Conclusions

Terrestrial Plants: Low risk for all uses

Birds and mammals

- *Foliar and soil uses:* Acute/chronic risk concerns for imi and clothi

- *Seed treatments:*
  - o Acute and chronic risk concerns for imi, clothi and thia
  - o Risk conclusions were refined considering seed size and % of diet to reach the level of concern
    - o Greatest potential risk for uses on small seeds that require only a few seeds to reach LOC (e.g., lettuce)
    - o Potential for risk for large seeds that require only a few seeds to reach LOC, but seed size is too big for certain small species of birds (e.g., corn)
    - o Lowest potential risk for uses with large seeds that require more seeds to reach LOC
  - Dino is not registered for seed treatment

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For birds and mammals, acute and chronic risk was identified for foliar and soil uses for IMI and CLOTHI and seed treatment uses for IMI, CLOTHI, and THIA (note that DINO is not registered for seed treatments). For terrestrial plants, all uses were low risk.

Because the RQ approach assumes 100% of the avian/mammalian diet comes from seeds, the assessments refined risk conclusions based on seed size and % of diet to reach the level of concern. This allowed for certain use patterns to be grouped into a "higher risk" category for mitigation considerations. I'll note that we receive comments on the potential for exposure to spilled treated seed, most notable from the MN study that was recently published, that confirm the potential for seed treatment exposures.

The general conclusions are that
1. Seed size driving some conclusions:
Lettuce, sugarbeet, (only few needed, possible to be ingested)

2. Few seeds needed, but seed size too big (small/ed passerines)
Corn, soybean, cotton (small only)

3. Use Patterns and size class of lower concern
Larger percentage of diet, more seeds to consume

Tie back to SLUA, larger percentage of diet to reach LOC for major uses (corn, soybean, cotton)

Highlight relative ease of mitigating on small vegetable seeds (e.g. lettuce) by recommending bittering agent on seed coating

Uncertainties:
Terrestrial Risk: Assumes seed is palatable available for consumption

Aquatic Big Picture Risk Conclusions

Fish and Aquatic Plants: Low risk for all uses

Aquatic invertebrates

- *Foliar, Soil, Seed Treatment:*
  - Acute and chronic risk concerns for all 4 chemicals (some → most uses)
  - Note: risk concerns for dinotefuran in DRA based on lines of evidence other than RQs

There are acute and chronic risk concerns for all four chemicals and I'll note that chronic risks are the driver for aquatic invertebrates. For fish and aquatic plant risks are low.

New Data Set – Guelph (Raby *et al.*) Aquatic Invert Toxicity Data

- Large acute and chronic datasets across all 4 neonics (and acetamiprid)
- Acute data published Jan 2018; chronic data published July 2018
- Allowed for apples-to-apples comparison of toxicity data across the 4 neonics, accounting for lab and study conduct variability
- 22 species tested for acute, including a range of species' sensitivities and 2 most sensitive acute species tested for chronic
- Tested species did not include the most sensitive species identified for imidacloprid

We also received as part of the comment period data from Guelph, which has since been published. The Raby et al. study represents a large acute and chronic toxicity dataset across the four neonics (as well as acetamiprid) that allowed for an apples-to-apples comparison, accounting for lab and study conduct variability. There were 22 species included in the acute tests that included a range of species. The 2 most sensitive species from the acute test were then used in the chronic tests (the midge and a mayfly species). However, I'll note that the tested species did not include the most sensitive species identified for IMI.

Guelph Aquatic Invert Comparative Risk Conclusions

- Acute Toxicity
  - Imidacloprid similar to Clothianidin and Dinotefuran > Thiamethoxam
- Chronic Toxicity
  - Imidacloprid and Clothianidin > Dinotefuran > Thiamethoxam
- Acute and Chronic Risks
  - Comparison of risk incorporates varying chemical-specific application rates and aquatic modeling parameters
  - Imidacloprid, Clothianidin, and Dinotefuran have similar risk profiles (RQs within 10x)
  - Thiamethoxam presents lower risks

In response to receiving this data and to support potential mitigation options being considered by PRD, the team conducted two analyses: the first compared the acute and chronic toxicity of CLOTHI, THIA, and DINO to IMI and, since toxicity is only one part of the risk picture, the second analysis accounted for potential exposure to compare the acute and chronic risk of CLOTHI, THIA, and DINO to IM. The results of the toxicity comprison found that on an acute basis IMI is similar to CLOTHI and DINO and all three are more sensitive than THIA; on a chronic basis IMI is similar to CLOTHI and are more sensitive to DINO which is more sensitive than THIA. When this is translated into risk, IMI CLOTHI and DINO have similar risk profiles on an acute and chronic basis, while THIA presents a lower risk.

Aquatic Monitoring Data

- Sourced primarily from Water Quality Portal (multiple databases within)
  - Generally non-targeted in nature
  - Some targeted open literature data available for imidacloprid
- For imi, clothi, and thia:
  - Monitoring values similar to modeled data
  - Acute and chronic risk indicated

Chemical	# Samples	% Detection Frequency	Highest concentration (µg a.i/L)	Chronic Endpoint from Risk Assessment (µg a.i/L)	Chronic Endpoint from Raby et al (µg a.i/L)	% of Monitoring Values Exceeding Most Sensitive Endpoint
Imidacloprid	8,418	27%	12.7	0.01*	0.156**	14%
Clothianidin	1,801	12%	1.34	<0.5	0.31**	3%
Thiamethoxam	3,005	9%	4.37	0.74**	6.3**	0.13%
Dinotefuran	1,316	30%	11.7	10,000++	3.1**	0.23%

* Mayfly (*Caenis horaria*)
** Midge (*Chironomus dilutus*)
\+ Mayfly (*Neocloeon triangulifer*)
\++ Daphnid (*Daphnis magna*)

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In addition to the comparisons to modeled data, it is important to note that there is a substantial monitoring data set available for the neonics. It is mportant to note that there is overlap of observed monitoring values with modeled data as well as aquatic endpoints (especially when considering the Raby et al data). This supports the potential for exposure and effects in the environment.

Caveat % of monitoring values exceeding most sensitive endpoint: we are comparing a daily sampled value and may not be representative of a chronic exposure.

Strengths and Additional Considerations

Ex. 5 Deliberative Process (DP)

Back-pocket Slides

Purpose

- Provide OPP management with a summary of neonic risk conclusions
  - final bee risk assessments
  - aquatic and terrestrial taxa (non-bee) risk assessments
- Emphasize new methodology and response to public comments for final bee assessment
- Provide detailed scientific background prior to PRD's briefing on the neonic risk mitigation strategy

The goal of this presentation is to provide a summary of the neonic risk conclusions for the highly refined final bee and non-bee risk assessments with an emphasis on new methodology and response to public comments for the final bee assessments.

Outline of Presentation

- Final Bee Risk Assessments
  - o Approach for assessing risks to bees
  - o What's new since preliminary bee RAs
  - o Lines of evidence considered / strength of confidence calls
  - o Risk conclusions (low risk calls; weak, moderate, and strong evidence of risk calls)
- Recap of risk conclusions for aquatics and terrestrial (non-bee) taxa
  - New toxicity data analysis
- Conclusions
  - o Strengths and additional considerations of risk assessment approaches

Here is the outline for today's presentation. We'll go through the registration review timeline quickly before jumping into the final bee risk assessments; a recap of risk conclusions for the non-bee taxa, including the new toxicity analysis conducted with the Raby data; and walk through some final conclusions.

Preliminary Bee RAs - Major Public Comments

- Comments that were addressed through modification of the risk assessment
  - Criticism of "bee bread" method and alternative suggestions
  - Lack of non-agricultural use risk assessment
  - Assessments were not adequate due to numerous "Uncertain" calls
- Comments on lack of assessment for less-typical exposure routes
  - Seed dust, soil exposure, drinking water, guttation fluid
- Other substantive comments that did not result in changes to the risk assessment (not exclusive to neonics)
  - Assessments do not consider mixtures, cumulative effects, or synergy
  - Honeybees are not appropriate surrogates
  - Not enough consideration for studies that include sublethal effects or non-apical endpoints (*e.g.,* immunosuppression, foraging ability, biochemical changes)

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This slide summarizes the major categories of public comments received on the preliminary bee risk assessments. While these comments are generic to the four neonics being assessed, there are chemical-specific comments that have been incorporated into the risk assessments as appropriate. Major commenters were USDA, registrants, various crop groups, non-profits, and state agencies.

There were several comments that were addressed through modifications to the risk assessment. These included: criticism of the "bee bread" method and alternative suggestions for how to estimate exposure for the Tier II analysis. These comments informed development of the new method for estimating exposure. There were comments that the risk assessments did not consider non-ag uses; these uses are considered in the final assessments (risk calls will be discussed later). And finally, there were comments that the assessments were not adequate because of the numerous "uncertain calls". These calls in the preliminary assessments were due to gaps in the dataset, mainly for the tier II assessment. Since the drafts, we have received new colony feeding studies for the chemicals and residue data that have allowed us to update our higher tiered exposure assessment.

There were also comments on the lack of quantitative assessment for some of the less-typical exposure routes, such as, seed dust, soil exposure, drinking water, and guttation fluid. These routes are discussed qualitatively in the assessments both because the potential exposures are substantially less than those from dietary and contact exposure and because there aren't methods to quantify them. Of all of these less-typical routes, the most relevant is seed dust as there are numerous incidents associated with this type of exposure. This is being addressed through stewardship.

And finally, there are other substantive comments that did not result in changes to the risk assessments. These are not exclusive to neonics and, ultimately, are not persuasive. Most of them relate to policy decisions and are being addressed with other work (e.g., synergy).

Non-bee RAs – Major Public Comments

- Consumption of treated seeds by birds/mammals
  - Not sufficiently protective
    - Study from Univ of MN – > 25% of LD_{50} ingested, neurological signs
    - Study from Univ of Saskatchewan showing weight loss/disorientation
  - Too conservative
    - Single food source, max load, every day
- Consideration of synergistic/cumulative effects of neonicotinoids
- Increased consideration of monitoring data, only consider habitats suitable for aquatic organisms, don't use foreign data
- Underestimation of runoff from treated seeds
- No accounting for residential uses and impacts to POTWs

EPA received several comments on the aquatic and terrestrial (non-bee) taxa, including those related to consumption of treated seeds, consideration of synergistic and cumulative effects, monitoring data, underestimation of runoff from treated seeds, and impacts from residential uses on POTWs,

[Not sure if treated seeds data were considered

Monitoring data – monitoring data not sampled frequently enough to use alone. Habitats may discharge into receiving waterbodies that do harbor aquatic organisms. Foreign data provide line of evidence that neonics can contaminate waterbodies.

Underestimation of seed runoff - new seed treatment memo, EECs revised

Residential uses on POTWs – use of down-the-drain model require production volumes, can't parse out what is used for ag purposes and what is used for residential uses. Consider ag EECs as surrogates for residential uses when looking at mitigation options.]

Seed Treatment Residue Bridging – Conclusions

- Crop specific 90th percentile values (from all trials) were used:
  - Separate values for corn, cotton, soybean and canola
    - Data bridged across chemicals
  - Tier I (refined)
  - Tier II (when needed)
- For crops with no seed treatment residue studies, available data for corn, cotton, canola and soybean were used to bridge to other crops
  - 90th percentiles used for all other crops, with adjustments for treatment rate

The recommendations based on the seed treatment bridging that were used in the risk assessments were: 1) for crops with available data, use the 90th percentile value from all chemicals. There are separate values for corn, cotton, soybean, and canola. These values are used to refine Tier I estimates, and Tier II only when needed (which was not very often). 2) for crops without data, the aggregate 90th percentile across all of the crops (i.e., corn, cotton, canola, and soybean) is used.

[90th percentile is the high end year/site conditions. 90th selected based on policy and level of protection we tend to pick. Consistent with aquatic EECs. Precedent.]

Foliar and Soil Bridging – Conclusions

- Based on the bridging analysis, the following crop/crop groups are bridged across chemicals:
  - Cotton (THIA only)
  - Cucurbits
  - Orchards (Stone fruit, pome fruit, citrus, tree nuts, tropical fruit)
  - Berries and small fruits
  - Fruiting vegetables (*e.g.,* peppers)
  - Soybeans
- For crops/crop groups with insufficient data:
  - Cotton and cucurbit data used as surrogates
  - Relevant crop groups
    - Root and tuber (*e.g.,* sweet potato)
    - Fruiting vegetables (*e.g.,* okra and roselle)
    - Herbs and spices

Based on the bridging analysis for foliar and soil applications, cotton, cucurbits, orchards, berries and small fruits, and soybeans are bridged across all chemicals. A few things to note: cotton data is bridged across chemicals for THIA only because there was sufficient data for IMI, CLOTHI, and DINO to use chemical-specific data. Orchards represents an artificial grouping of various tree crop groups (e.g., citrus, stone, pome, tree nut). Residues are bridged across all orchard crop groups.

For crops/crop groups with insufficient data, using other crops as surrogates we have enough data to cover most of the crops that are registered with some degree of confidence.

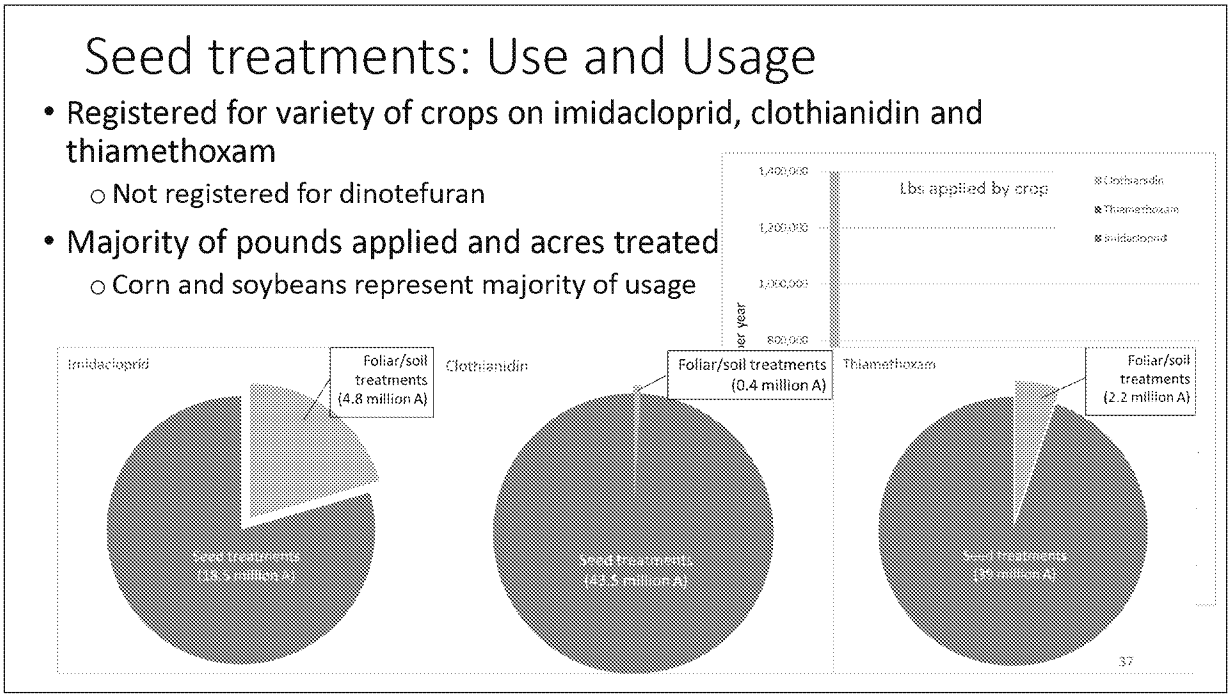
{HED didn't have any issues with approach}

Non-Ag Bridging – Conclusions

- Limited Ornamental data were available for imidacloprid, dinotefuran and thiamethoxam
  - Imidacloprid and Dinotefuran data were not comparable to other a.i.'s due to the way their application rates were described in study reports.
  - Thiamethoxam data were used as surrogates for all other a.i.'s
  - Residues in nectar alone from foliar applications = 100 - 1000s ppb
  - Residues in nectar alone from soil applications = 10 - 100s ppb
- Open Literature residue data on Turf for imidacloprid and clothianidin suggested the a.i. are similar with very high initial concentrations (>1000 ppb), but with rapid declines (~20 ppb by 3 weeks)

For the non-ag bridging there were limited ornamental data available for imidacloprid, dinotefuran, and thiamethoxam; however, the IMI and DINO data were not comparable to each other or THIA because of the application methods/rates described in the studies (e.g., soil injections described on a lbs a.i./m plant height basis). Based on the conclusions from the foliar and soil bridging analysis for agricultural crops that chemical did not greatly influence residues and that the residues from the ornamental species were in the PPM range, we used the THIA foliar and soil data as surrogates for all other chemicals.

For turf we were focusing on the less-managed residential turf that contains bee-attractive plants such as clover. Data for this scenario was available from one open literature study for imidacloprid and clothianidin, which suggested similar initial residues in clover in the PPM range that rapidly declines to the low PPB range within 3 weeks of application.



Starting with use and usage. Seed treatments are registered for a variety of crops on IMI, CLOTHI, and THIA. They are not registered for DINO. The three pie graphs show the average acres treated (calculated by multiplying acres grown by average PCT from SLUA)of seed treatments versus all other uses registered for IMI, CLOTHI, and THIA. These highlight just how much of the use is seed treatment, which, spoiler alert, is mostly considered low risk. However, it is important to note that numerous bee kill incidents have been associated with dust-off for each chemical: IMI has 5 reported incidents (canola, corn, soybean) from 2006 to 2016; THIA has 2 reported incidents that we can associate with seed treatment in the US (IN and MN- the magnitude of these incidents is on the order of thousands of hives) in 2012 with additional international incidents. It is possible that some of the other reports were associated with seed treatment, but we cannot confirm due to lack of details in the reports. CLOTHI has 18 incidents (corn or general ag areas) from 2010 to 2016 with numerous additional international incidents.

These incidents highlight the potential for effects and the large spatial scale of these uses.

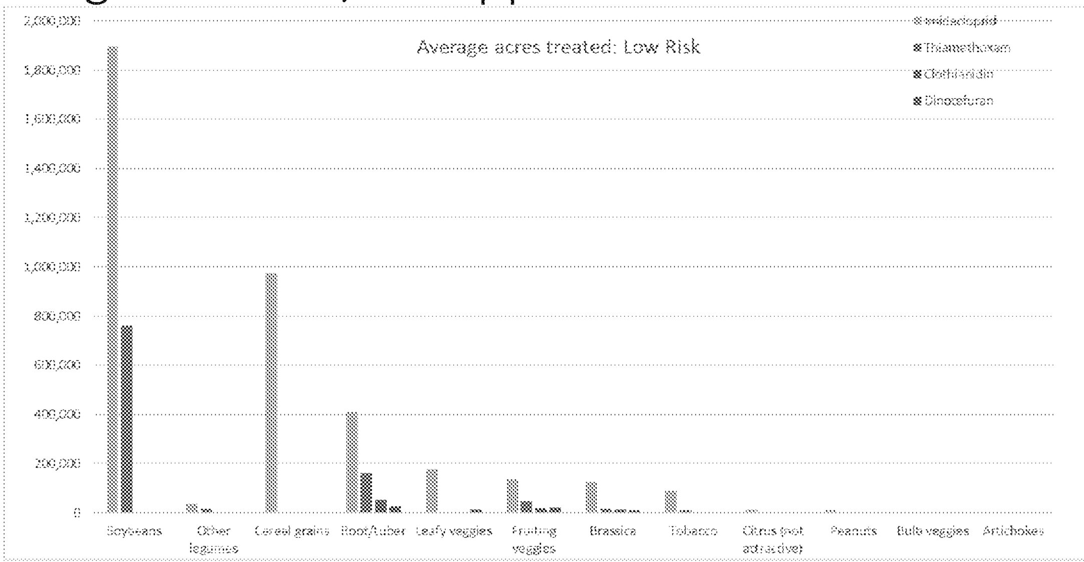
To get a sense for the specific crops with the greatest usage we have the figure on the right, which shows the lbs applied for each chemical by crop. Corn and soybean pop out as representing the majority of the usage.

LOW RISK crops - For foliar/soil aps, the most usage is on soybeans, cereal grains.

RISK crops - There are some nuances to consider, but for foliar/soil aps, the crops with the highest acres treated are cotton, berries, and citrus. The acreage for the risk crops is substantially less than the acreage for the low risk crops.

[For some of the orchard crop data, it is unknown whether usage was pre- or post- bloom. So, some of these acres treated may be green. E.g., clothi use on pome stone and tree nuts.]

Usage for foliar/soil applications



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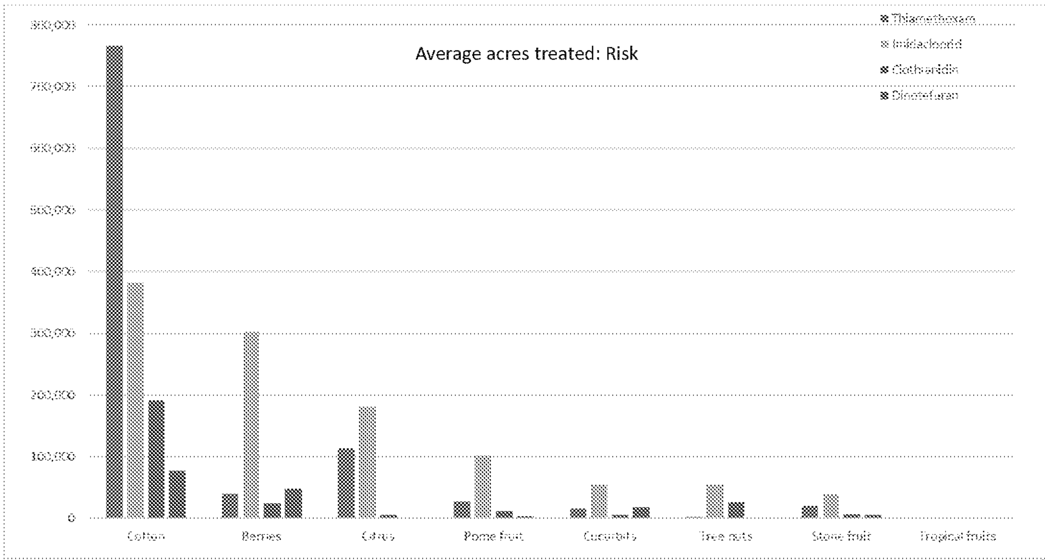
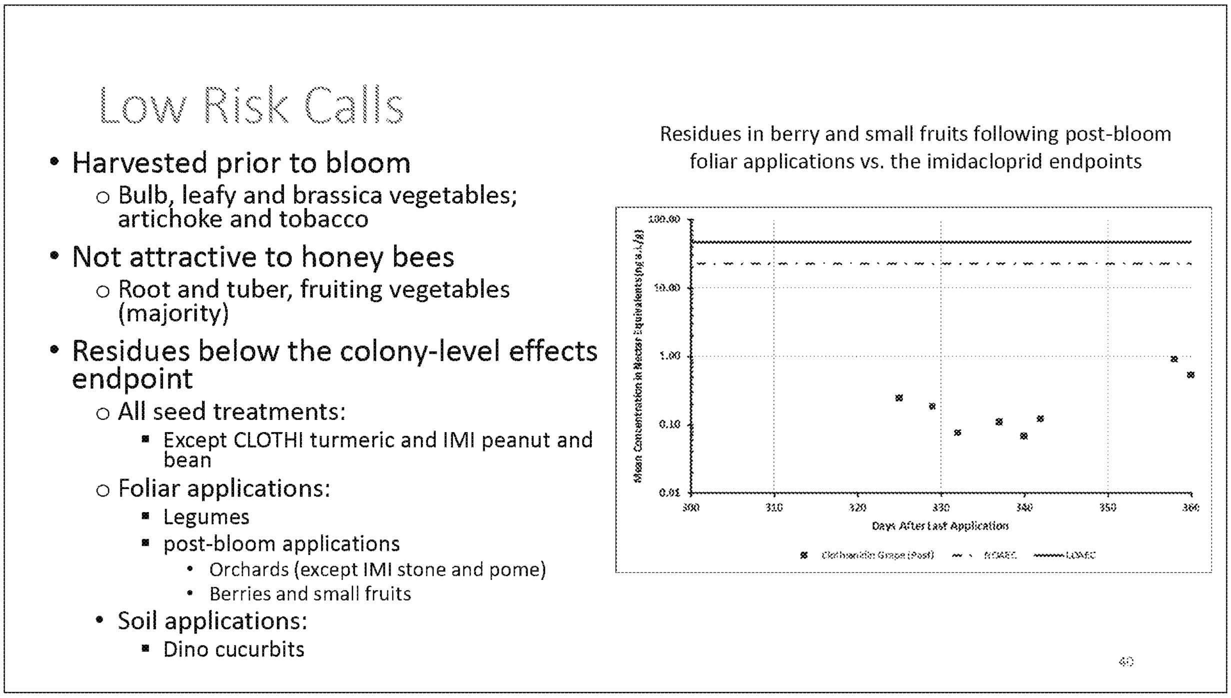
Moving on to the foliar and soil applications, this figure shows the average acres treated (calculated the same was as for seed treatments) for all of the low risk crops/crop groups. For foliar/soil aps, the most usage is on soybeans, cereal grains. Take note of the y-axis before we transition to the next slide.

Usage for foliar/soil applications



This shows the average acres treated for the risk crops. These data are for uses that have at least one red risk call so there are some nuances that don't translate, but in general, the crops with the highest acres treated are cotton, berries, and citrus. If you recall the scale from the previous slide you can see that the acreage for the risk crops is substantially less than the acreage for the low risk crops.

[For some of the orchard crop data, it is unknown whether usage was pre- or post- bloom. So, some of these acres treated may be green. E.g., clothi use on pome stone and tree nuts.]



Crops/crop groups were considered low risk because they were harvested prior to bloom (e.g., bulb, leafy and brassica vegetables; artichoke and tobacco), not considered attractive to honey bees (i.e., certain crops within the root and tuber and fruiting vegetables crop groups), or had measured residues below the colony-level effects endpoints. The figure on the right is an example for foliar post-bloom applications to berry and small fruit crops where the residues are substantially lower than the imidacloprid colony level NOAEC and LOAEC.

Risk Calls

- Cotton
  - Foliar: IMI; CLOTHI; THIA; DINO
  - Soil: IMI
- Cucurbits
  - Foliar: CLOTHI; THIA; DINO
  - Soil: IMI; CLOTHI, THIA
- Orchards
  - Foliar Pre-bloom: IMI; CLOTHI; THIA; DINO
  - Foliar Post-bloom: IMI (except tree nuts)
  - Soil Pre-, Post-bloom: IMI; CLOTHI; THIA
  - Soil Pre-bloom: DINO
- Berries and Small Fruits
  - Foliar Pre-bloom: IMI; CLOTHI; THIA; DINO
  - Soil Pre-bloom: IMI; THIA; DINO
- Legumes
  - Soil: IMI
- Other Herbaceous Crops
  - Root and Tuber
  - Fruiting Vegetables
  - Herbs and Spices
- Seed Treatments
  - Turmeric: CLOTHI
  - Bean and Peanut: IMI
- Ornamentals and Forestry
  - Foliar/Soil: IMI; CLOTHI; THIA; DINO
  - Trunk Injection: IMI; DINO
- Turf (residential)

Moving to the risk calls… We'll walk through the details in the following slides, but risk calls were made for all of the uses shown here. As discussed previously, risk calls are based on residue values exceeding the NOAEC. However, all of the lines of evidence were used to characterize the strength of the risk call.

Risk Calls- Cotton Foliar

Lines of Evidence	Imidacloprid		Clothianidin		Thiamethoxam		Dinotefuran
Residue Data	CS		CS		B		CS
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC*
Frequency (# of daily mean residues > endpoint)	2 (FN) 0 (XFN)	0 (FN) 0 (XFN)	8 (FN) 28 (XFN)	4 (FN) 26 (XFN)	0 (FN) 4 (XFN)	0 (FN) 2 (XFN)	2 (FN) 11 (XFN)
Magnitude (Ratio of max residue to endpoint)	**1.1X** (FN) **1.5X** (XFN)	0.5X (FN) 0.7X (XFN)	**7.7X** (FN) **412** (XFN)	**4.0X** (FN) **220X** (XFN)	0.24X (FN) **3.4X** (XFN)	0.12X (FN) **1.7X** (XFN)	**9.7X** (FN) **177X** (XFN)
Duration (# of days > endpoint)	20 (FN) 22 (XFN)	8 (FN) 7 (XFN)	9 (FN) 49 (XFN)	7 (FN) 49 (XFN)	8 (FN) 20 (XFN)	6 (FN) 17 (XFN)	10 (FN) 35 (XFN)
Incidents	None		3 honey bee kills		None		None

Additional considerations for cotton:

- Considered attractive for floral nectar, potentially attractive for extrafloral nectar, and not attractive for pollen
- Has an indeterminant bloom period
- Does not require managed pollinators but used for honey production by some commercial beekeepers

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CS = Chemical Specific Data, B=Bridged Data

The next few slides have a similar format so I will take some time to orient folks. These tables summarize the information included in the lines of evidence tables presented in the Tier II risk characterizations. The rows are the lines of evidence, including, whether risk conclusions are based on chemical specific residues, bridged residues, or both; the endpoint under consideration (NOAEC or LOAEC); the frequency of exceedances based on the number of daily mean residues that are greater than the endpoint [note, we are presenting absolute number of residues exceeding, but it is important to note that some have a lot of data and some don't]; the magnitude of the exceedances as presented by the ratio of the max residue to the endpoint; the duration of exceedances; and the incidents. The columns are the individual chemicals. I know they don't look it, but these tables are actually pretty high level and roll up a lot of information. The nuances are described in the documents.

A few considerations: Given the importance of the THIA degradate (i.e., CLOTHI), residue data are typically compared to both the thia and clothi endpoints (you'll see these presented in parentheses in the following slides). However, for cotton we are not considering the clothi endpoints due to low percent of clothi present in studies with thia. A definitive LOAEC is not available for DINO, but based on transient effects observed at the NOAEC for all of the neonics, the LOAEC is likely with a factor of 5X the NOAEC.

Ok so moving into the risk call for cotton. pollen is not considered honeybee attractive so it is not considered in the residues (i.e., we did not calculate a total concentration in diet based on the method described previously). Somewhat unique to cotton, is that plants produce both floral nectar and extrafloral nectar. Extrafloral nectar is basically nectar produced by the plant from nectaries that occur on stems rather than flowers. It is produced even when the plant is not flowering. While floral nectar is considered honey bee attractive, the attractiveness of extrafloral nectar is uncertain. However, based on similarities in composition [and a few open literature sources], it is reasonable to assume bees are attracted to extrafloral nectar, though the extent and duration of its use is uncertain. For the purposes of the risk assessment, we present risks for both floral and extrafloral nectar.

As mentioned previously. There was sufficient data to conduct monte carlo analyses based on chemical-specific data for IMI, CLOTHI, and DINO, while THIA relies on bridged data from the other three chemicals. In general, the frequency, duration, and magnitude of exceedances are greater for extrafloral nectar than floral nectar. Cotton does not require managed pollinators but commercial beekeepers do utilize cotton fields for their hives so there is potential for exposure. And there are confirmed incidents for CLOTHI that indicate this is a relevant route of exposure.

There is strong evidence of risk based on magnitude of exceedances (up to 412 for extrafloral nectar) and duration of exceedances (from weeks to months).

Risk Calls- Cucurbit Foliar

Lines of Evidence	Clothianidin		Thiamethoxam*		Dinotefuran
Residue Data	CS, B		CS, B		B
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC*
Frequency (# of daily mean residues > endpoint)	15	12	8 (14)	5 (10)	3
Magnitude (Ratio of max residue to endpoint)	**15.6X**	**8.3X**	**5X (11X)**	**2.5X (6.3X)**	**3.2X**
Duration (# of days > endpoint)	26	17	16 (22)	6 (13)	15
Incidents	None		None		None

Additional considerations for cucurbits:
- Considered highly attractive for nectar and pollen
- Has an indeterminant bloom period
- Requires managed pollinators

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

Here is the lines of evidence table for foliar applications to cucurbits. Note that imi is not registered for foliar applications which is why it is not in the table and we are presenting results for thia based on both the thia and clothi endpoints.

Cucurbits are pollinator attractive and do use managed pollinators. There are no reported incidents.

There is strong evidence of risk for clothi and thia based on exceedance of chemical-specific and bridged residues, the magnitude of those exceedances (up to 15x), and the number of days above the endpoint on the order of weeks. For DINO the residues exceed the bridged residue only and the magnitude of exceedance is lower, so the evidence of risk isn't as strong. [Dino-specific data are not suitable for use in risk assessment because the nectar and sometimes pollen were collected from in-hive sources].

Risk Calls- Cucurbit Soil

Lines of Evidence	Imidacloprid		Clothianidin		Thiamethoxam*	
Residue Data	CS, B		CS, B		CS, B	
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC
Frequency (# of daily mean residues > endpoint)	25	9	13	7	1 (9)	0 (1)
Magnitude (Ratio of max residue to endpoint)	**5.5X**	**2.7X**	**3.6X**	1.1X	0.69X (**1.5X**)	0.57X (**1.4X**)
Duration (# of days > endpoint)	67	57	57	47	34 (47)	0 (34)
Incidents	None		None		None	

Additional considerations for cucurbits:
- Considered highly attractive for nectar and pollen
- Has an indeterminant bloom period
- Requires managed pollinators

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

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Moving on the soil applications to cucurbits. Note dino soil applications are considered "low risk", which is why its not in the table.

Compared to the foliar applications, the magnitude of exceedances are lower, but the duration of those exceedances is much longer (months vs. weeks) This will be a common theme for the crop groups with both foliar and soil applications.

Risk Calls- Orchards Foliar

Lines of Evidence	Imidacloprid				Thiamethoxam*		Dinotefuran
Application Timing	Pre-bloom (Citrus)		Post-bloom (Stone/Pome)		Pre-bloom		Pre-bloom
Residue Data	CS, B		CS, B		CS, B		B
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC*
Frequency (# of daily mean residues > endpoint)	24	22	4	0	20 (23)	11 (21)	8
Magnitude (Ratio of max residue to endpoint)	**166**X	**80**X	**1.5**X	0.7X	**33**X (**76**X)	**19**X (**47**X)	**16.6**X
Duration (# of days > endpoint)	46	34	200+	0	35 (35)	18 (27)	14
Incidents	2 bee kill incidents on orchard crops				13 bee kill incidents on orchard crops		None

Additional considerations for orchards:

- Considered attractive or highly attractive for nectar and pollen
- Bloom duration varies by crop and variety
- Requires managed pollinators and used for honey production by some commercial beekeepers

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

Here is the risk table for foliar applications to orchards. Not that pre-bloom and post-bloom applications are included for imi, while post-bloom applications for thia and dino are considered low risk. Also note that Clothi is not registered for pre-bloom foliar applications.

Orchards are considered attractive to highly attractive, require managed pollinators and may be used for honey production by some commercial beekeepers. There is strong evidence of risk for imi and thia pre-bloom application based on exceedance of chemical-specific and bridged residues, the magnitude of those exceedances (up to 166x for NOAEC and 80x for LOAEC), and the number of days above the endpoint on the order of months. There are also reported incidents for both imi and thia that confirm the route of exposure. While the incidents are not tied to a particular application method or timing, based on the measured residues it is reasonable to infer they are the result of foliar applications.

Risk Calls- Orchards Soil

Lines of Evidence	Imidacloprid		Clothianidin		Thiamethoxam*	
Application Timing	Soil: Pre-/Post-bloom		Soil: Pre-/Post-bloom		Soil: Pre-/Post-bloom	
Residue Data	CS, B		CS, B		CS, B	
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC
Frequency (# of daily mean residues > endpoint)	63	24	23	12	5 (16)	1 (8)
Magnitude (Ratio of max residue to endpoint)	**3.6-19X**	**1.7-8.9X**	**9.1X**	**4.8X**	**2.7X (6.5X)**	**1.5X (3.5X)**
Duration (# of days > endpoint)	186	179	180	156	60 (156)	20 (156)
Incidents	2 bee kill incidents on orchard crops		None		13 bee kill incidents on orchard crops	

Additional considerations for orchards:

- Considered attractive or highly attractive for nectar and pollen
- Bloom duration varies by crop and variety
- Requires managed pollinators and used for honey production by some commercial beekeepers

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

Now for soil pre and post bloom soil applications to orchards. Dino soil applications are considered LOW risk so they are not presented here.

As we've seen with other soil applications, the magnitude of exceedances are lower than foliar (up to 19x for NOAEC and 8.9x for LOAEC), but the duration of those exceedances is much longer (up to 6 months in some cases).

Risk Calls- Berries and Small Fruits Foliar (Pre-bloom)

Lines of Evidence	Imidacloprid		Clothianidin		Thiamethoxam*		Dinotefuran
Application Timing	Pre-bloom		Pre-bloom		Pre-bloom		Pre-bloom
Residue Data	B		CS		CS, B		CS, B
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC*
Frequency (# of daily mean residues > endpoint)	42	39	4	3	32 (37)	23 (33)	36
Magnitude (Ratio of max residue to endpoint)	**63X**	**30X**	**3.4X**	**1.8X**	**20X (50X)**	**12X (28X)**	**25X**
Duration (# of days > endpoint)	57	45	37	37	23 (31)	19 (24)	41
Incidents	None		None		None		None

Additional considerations for berries and small fruits:

- Considered attractive or highly attractive for nectar and pollen
- Bloom duration varies by crop and variety
- Requires managed pollinators and used for honey production by some commercial beekeepers

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

Here are the lines of evidence for pre-bloom foliar applications to berries and small fruits. Note that CLOTHI is only registered for pre-bloom applications to grapes. All post-bloom foliar applications are considered low risk.

Berries and small fruits is a diverse group, but for the most part crops are considered attractive to highly attractive for nectar and pollen, require managed pollinators, and may be used for honey production. Bloom duration varies but is at least a couple of weeks. There is strong evidence of risk for all chemicals. Duration of exceedances on the order of months.

Risk Calls- Berries and Small Fruits Soil (Pre-bloom)

Lines of Evidence	Imidacloprid		Thiamethoxam		Dinotefuran
Application Timing	Pre-bloom		Pre-bloom		Pre-bloom
Residue Data	B		CS, B		B
Endpoint	NOAEC	LOAEC	NOAEC	LOAEC	NOAEC*
Frequency (# of daily mean residues > endpoint)	15	14	5 (11)	2 (8)	4
Magnitude (Ratio of max residue to endpoint)	**21X**	**9.9X**	**3.2X (7.7X)**	**2.7X (6.1X)**	**2.4X**
Duration (# of days > endpoint)	83	83	83	83	60
Incidents	None		None		None

Additional considerations for berries and small fruits:

- Considered attractive or highly attractive for nectar and pollen
- Bloom duration varies by crop and variety
- Requires managed pollinators and used for honey production by some commercial beekeepers

*() Based on CLOTHI endpoints

CS = Chemical Specific Data, B=Bridged Data

Moving to pre-bloom soil applications. Again, clothi is only registered for pre-bloom applications to grape and is considered LOW risk based on chemical-specific residue data. For the other chemicals, risk is indicated. Again, the magnitude of exceedances are lower than foliar, but those exceedances occur for about twice as long.

Risk Calls- Berries and Small Fruits Soil (Post-bloom)

- Risk indicated for CLOTHI and THIA
- Conflicting lines of evidence
  - Residues of IMI in blueberry below colony-level endpoints
  - Residues bridged from orchards exceed colony-level endpoints

Risk was also indicated for post-bloom soil applications for clothi and thia only. However, this is based on conflicting lines of evidence and would be an example of weak evidence of risk.

Risk Calls – Other Herbaceous Crops

- Members from Fruiting Vegetable[1], Root/Tuber[1], Herbs and Spices crop groups producing honeybee attractive pollen and nectar
  - Honeybee attractive crops include: **sweet potato, okra, herbs and spices, roselle**
  - Potential for Risk for all chemicals is bridged from all herbaceous plant data including, cotton and cucurbits
    - Based on plant relationships (*e.g.* at the family level)
    - High risk is indicated for both cucurbit (foliar and soil) and oilseed crops (foliar)
    - For pre-bloom neonic applications residues exceed colony level endpoints
- Members from Fruiting Vegetable[1] crop group producing honeybee attractive pollen only
  - Honeybee attractive crops include: **Chili peppers**
  - Potential for Risk for all chemicals is bridged from fruiting vegetable data including, tomato, bell and chili pepper
    - Based on plant relationships (*e.g.* at the genus level)
    - Foliar – Pollen residues in tomato for thia and dino exceed colony level NOAECs
    - Soil – Pollen residues in bell pepper, chili pepper, and tomato exceed colony level NOAECs
    - Supported by exceedances in other crop groups

[1] the majority of crops in these groups are harvested prior to bloom or are not attractive to honeybees. These are generally bumblebee attractive.

In addition to the crop groups already discussed, there are a variety of other herbaceous crops that are considered honeybee attractive, including sweet potato, okra, roselle, chili peppers, and herbs and spices. Given the lack of crop-specific residues, data are bridged to other crops/crop groups based on taxonomic relationships (e.g., family or genus level similarities). Risk is indicated based on surrogate residue values exceeding the colony level endpoints.

These crops do not use managed pollinators.

Risk Calls – Seed Treatment Uses

- Turmeric (CLOTHI); bean and peanut (IMI)
  - Residues reflect a high-end estimate (e.g., 90th percentile);
  - Estimate derived from multiple crops and neonicotinoids, and
  - IMI- residues are between the colony-level NOAEC and LOAEC
  - CLOTHI- uncertain how representative residue data are for treated root/rhizome

There are also a few seed treatment uses that exceed the risk threshold; however there are uncertainties associated with those calls, including residue values falling between the colony-level NOAEC and LOAEC for IMI uses on bean and peanut, and how representative available residue data are for treated root/rhizome as in the case for CLOTHI use on turmeric.

Data Bridging Needs vs. Available Data--Foliar

Crop Group	Chemical (Foliar Application)			
	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Root/Tuber Vegetables		Potato		
Legumes	Soybean		Soybean	
Cucurbits	Watermelon	Pumpkin	Pumpkin, Cucumber	Pumpkin, Cucumber
Citrus Fruits	Orange		Orange	
Pome Fruits	Apple	Apple	Apple	
Stone Fruits	Cherry, Peach, Plum, Apricot	Peach	Cherry, Peach, Plum	Cherry, Peach
Berries/Small Fruits		Grape	Strawberry, Blueberry, Cranberry	Blueberry, Cranberry
Cereal Grains			**	***
Tree nuts	*	Almonds		
Oilseed	Cotton	Cotton	Cotton	Cotton
Fruiting Vegetables	Tomato		Tomato	Tomato

* Except almond for IMI; ** registered for barley only (not bee attractive); *** registered for rice only (not bee attractive)

Data Bridging Needs vs. Available Data--Soil

Crop Group	Chemical (Soil Application)			
	Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Root/Tuber Vegetables		Potato		Potato
Legumes				
Cucurbits	Melon, Watermelon	Melon, Pumpkin, Cucumber, Squash	Melon, Pumpkin, Cucumber, Squash	Melon, Pumpkin, Cucumber, Squash
Citrus Fruits	Orange, Mandarin, Grapefruit	Orange, Lemon	Orange	
Pome Fruits	Apple			
Stone Fruits	Cherry, Peach, Plum, Apricot			
Berries/Small Fruits	Strawberry, Blueberry	Grapes	Strawberry	
Cereal Grains		Corn**		
Tree nuts	*			
Oilseed	Cotton			
Fruiting Vegetable	Tomato		Pepper, Tomato	Pepper

* Except almond for IMI; ** Experimental Use permit for in-furrow soil application for corn.

Data Bridging Needs vs. Available Data—Seed and Trunk Injection

Crop Group	Application Method	Chemical			
		Imidacloprid	Clothianidin	Thiamethoxam	Dinotefuran
Root/Tuber Vegetables	**Seed**				
Legumes	**Seed**	Soybean	Soybean	Soybean	
Cucurbits	**Seed**	Melon*	Melon*		
Cereal Grains	**Seed**	Corn	Corn	Corn	
Forage, fodder, straw, hay (alfalfa)	**Seed**				
Peanut	**Seed**				
Oilseed	**Seed**	Sunflower, Canola	Cotton, Sunflower*, Canola	Cotton, Sunflower*, Canola	
Stone Fruit	**Trunk Injection**				Cherry

*only studies available are for European data

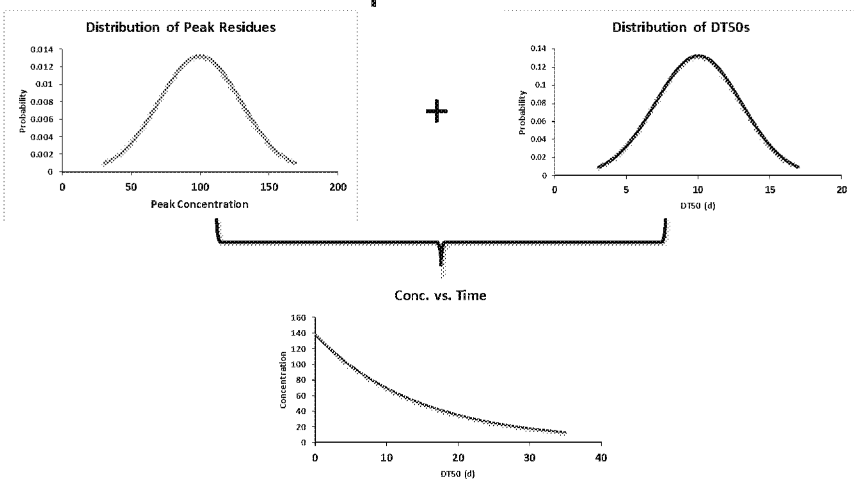
Seed Treatment Bridging Results

- Influence of site
  - For the same crop, residues are similar from site to site
- Influence of year
  - For some sites, residues are different from year to year
    - confidence intervals do not overlap
- Influence of chemical
  - Chemical does not appear to impact residue levels
  - Data can be bridged across chemicals
- Consideration of other plant tissues
  - Pollen and anthers – similar for corn
  - Pollen/nectar and flowers – same order of magnitude, but higher for soybean, cotton, canola
  - Pollen/nectar and leaves – order of magnitude higher for corn, soybean, cotton
- Influence of crop on concentrations
  - Residues in canola were higher than other crops

Foliar and Soil Residue Bridging

1. Estimate mean & variance of 2 parameters:
   - **A. Initial (peak) Concentration:** (C_initial)
   - **B. Dissipation rate:** (k)
2. Calculate dissipation curves associated with randomly sampled C_peak and k using Monte Carlo analysis (e.g., analogous to simulating 1000 fields). Select various "percentiles"
3. Use residue dissipation curve(s) for subsequent Tier 2 risk assessment

Monte Carlo simulation of residue dissipation curves

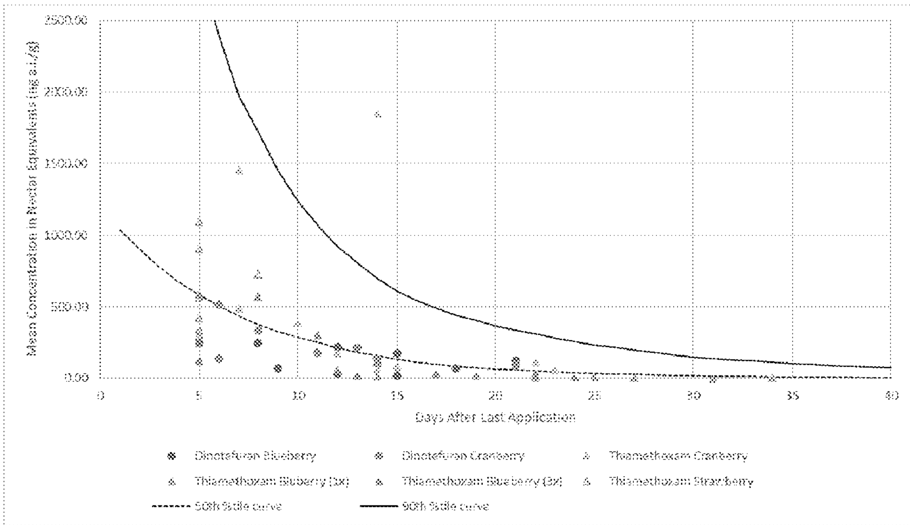


- Conceptually similar to EPA TREX approach (arthropod residues) & EFSA SHVAL tool for bee risk assessment, and HED tolerance analysis

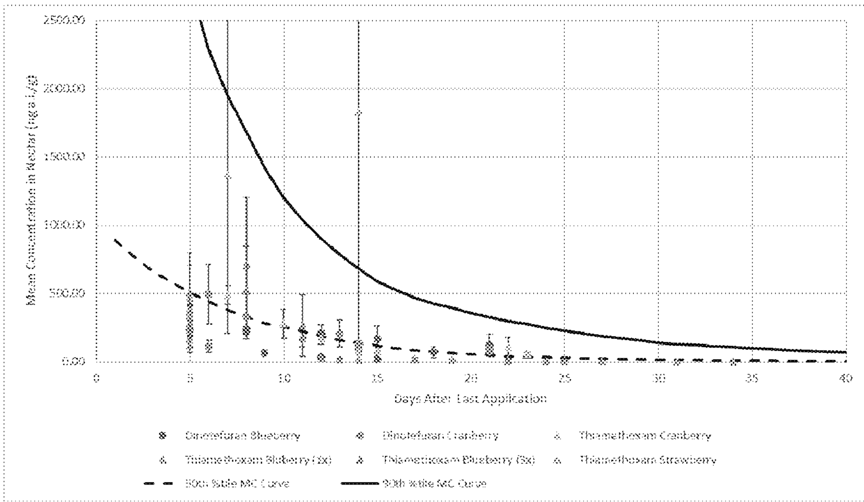
Simulation Components

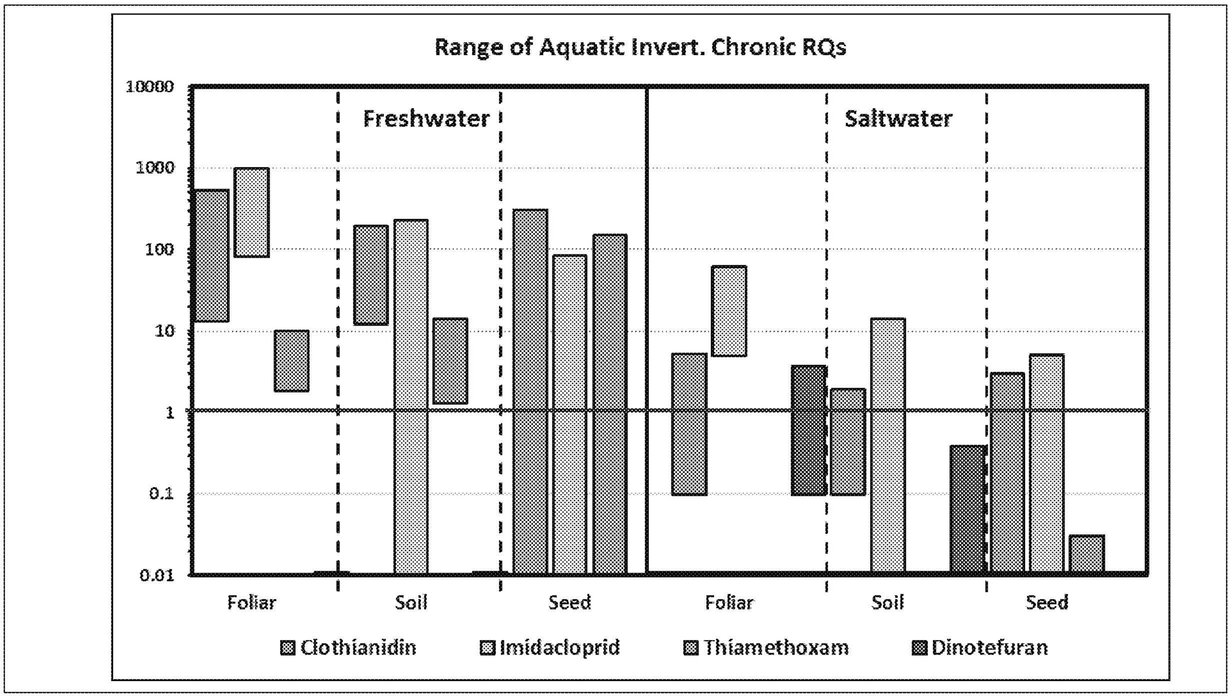
1. Select “k” mean, standard deviation (SD), Distribution type
2. Select C_initial mean, SD, distribution type
3. Set bounds around “k” and C_initial based on min and max of data
4. Based on distribution parameters of k and C_initial, randomly select values of k and C for each day of analysis (1000 times)
5. Calculate nectar equivalents based on new pollen method, # days to reach NOAEC, LOAEC
6. Plot risk curves for each matrix type along side of measured data.

Example Simulation: Berries foliar applications



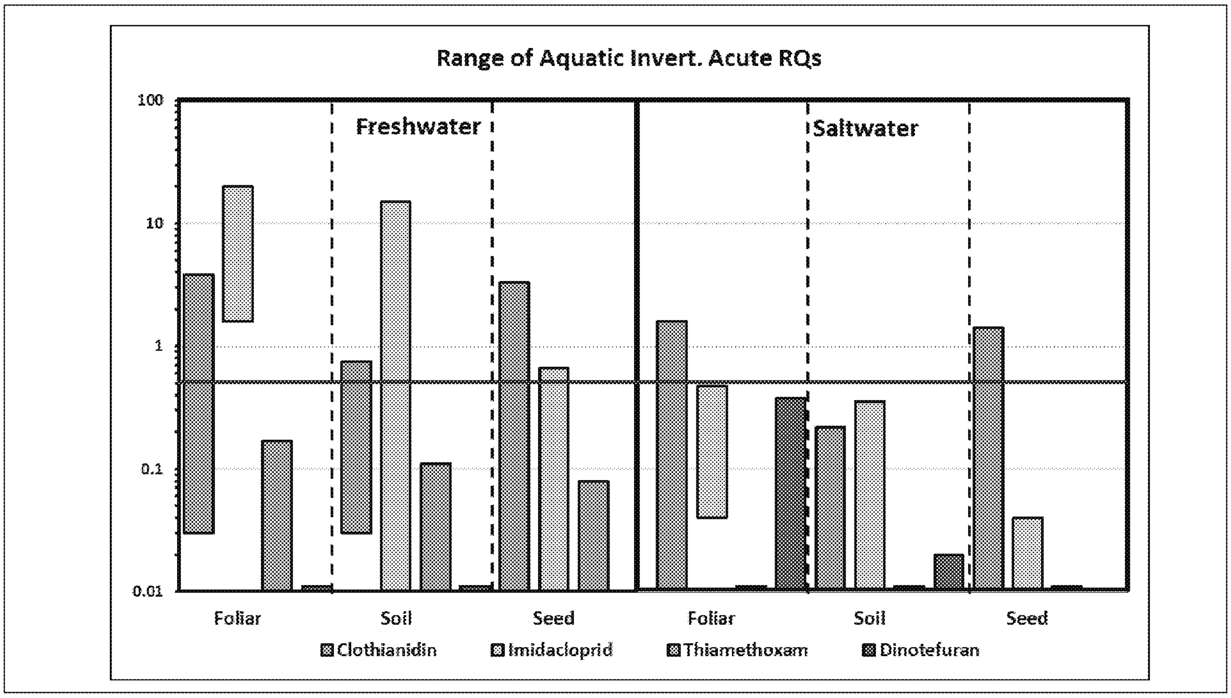
Example Simulation: Berries foliar applications





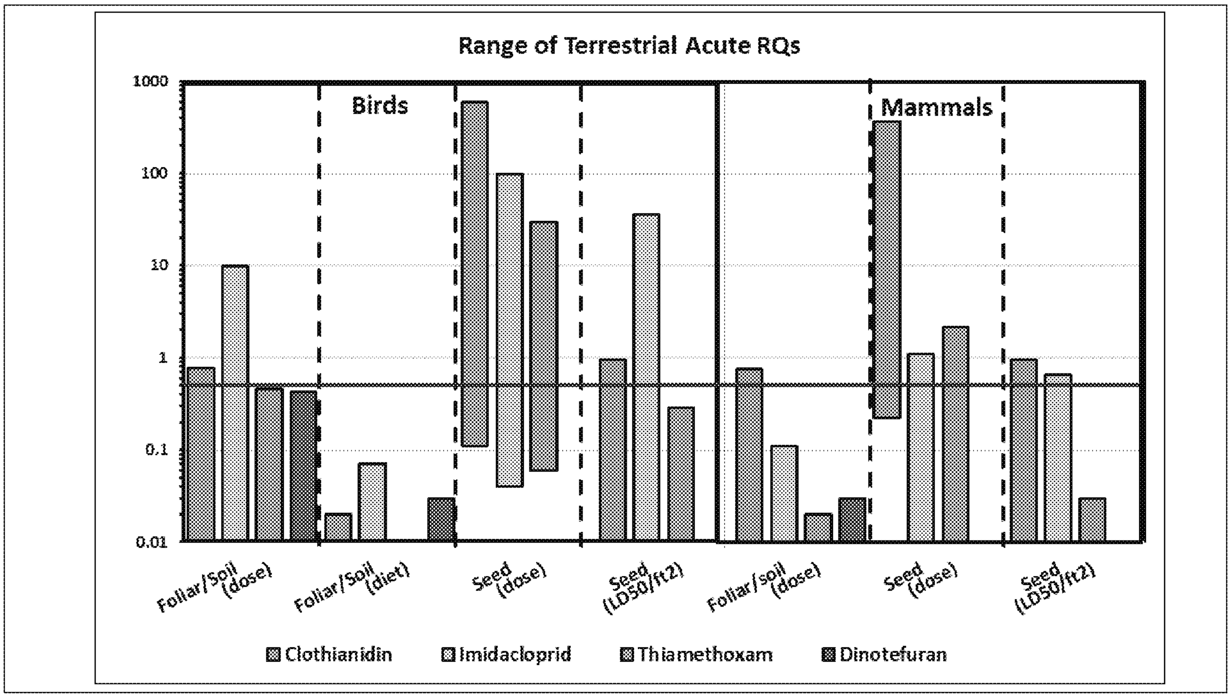
FW Inverts:
Foliar, Soil & Seed: Chronic risk indicated for clothi, Imi, thia;
Dino: no chronic risk (Daphnia)

SW Inverts:
Foliar, Soil & Seed: chronic risk indicated for clothi & imi;
Dino: chronic risk for foliar (rice, watercress)



FW Inverts (Non-listed):
Foliar: acute risk for clothi (rice only), imi (all uses)
Soil: acute risk for clothi (fruit/nut trees, poultry only), imi (many uses)
Seed: acute risk for clothi (rice only), imi, thia (rice only)

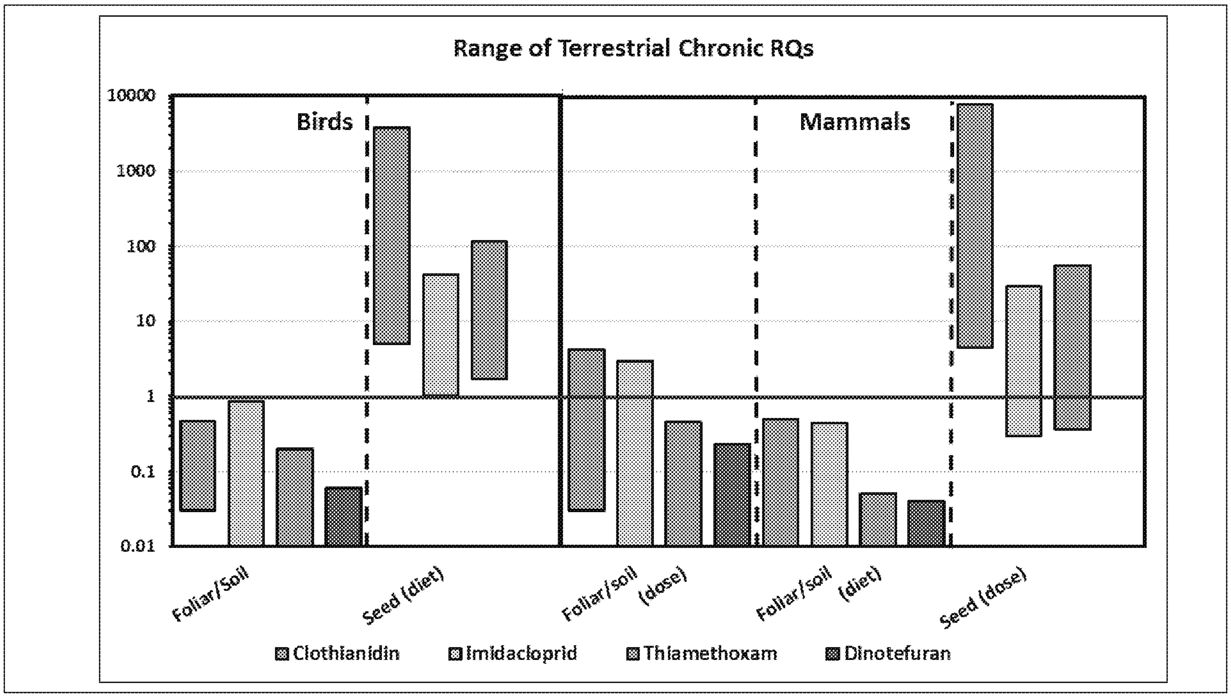
SW Inverts (Non-listed):
Foliar & Seed: acute risk for clothi (rice only)



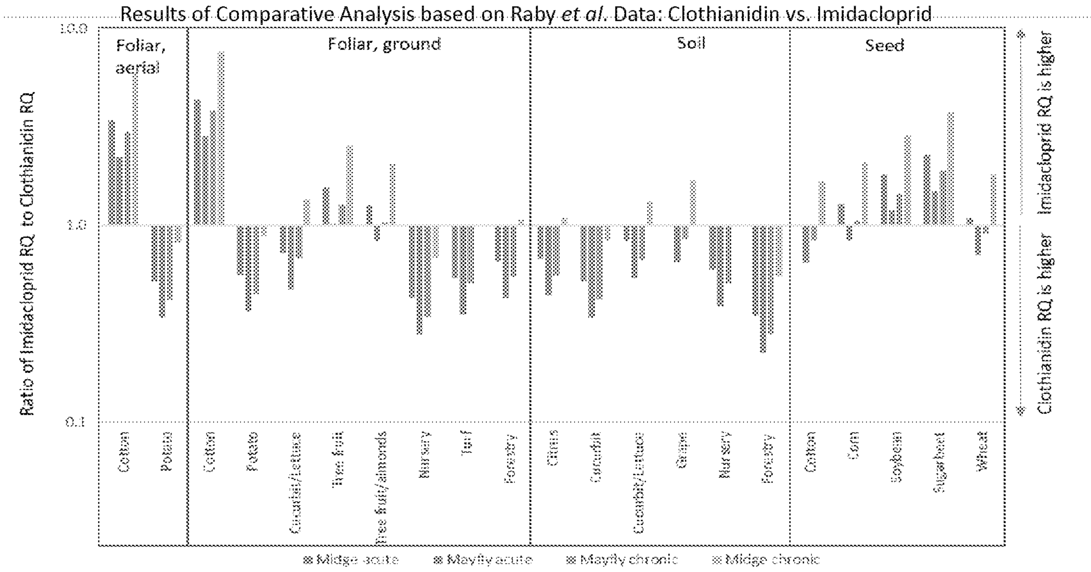
Application method breakdown, increase figure size

Do not highlight listed results, remove dotted lines

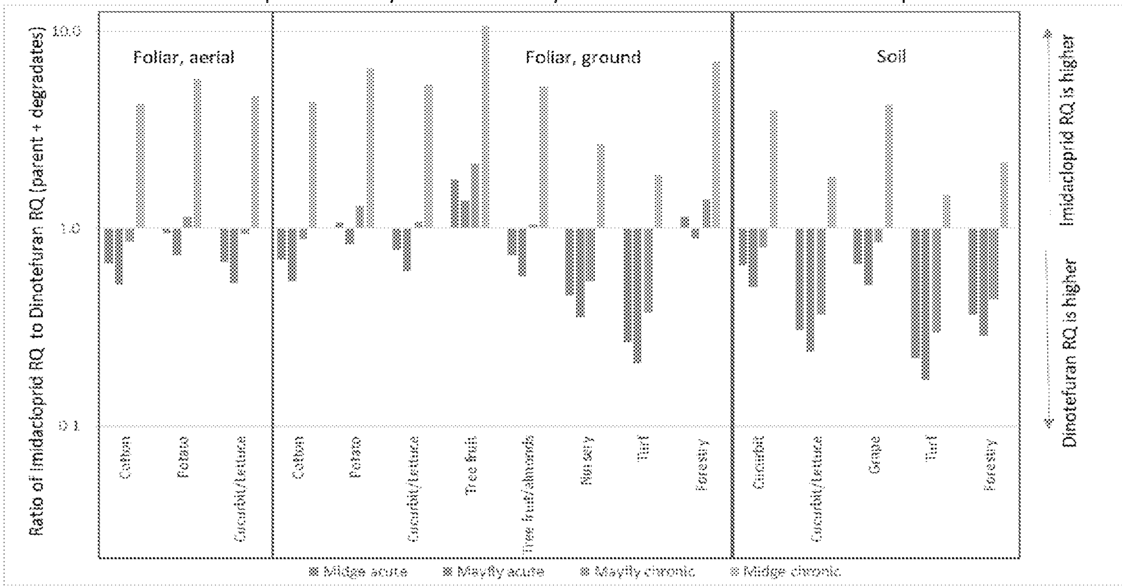
Big picture, marginal exceedances for foliar/soil, seed treatment driving risk concerns



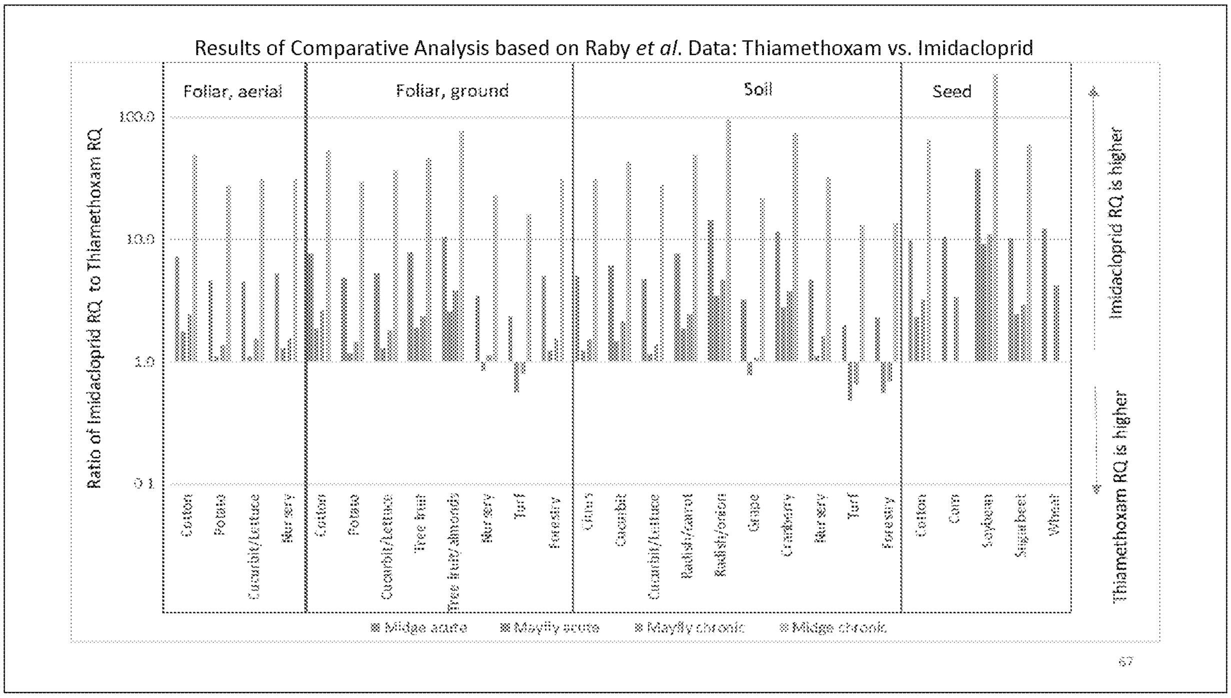
Same story as acute


Results of Comparative Analysis based on Raby et al. Data: Clothianidin vs. Imidacloprid
Ratio of Imidacloprid RQ to Clothianidin RQ
10.0
1.0
0.1
Foliar, aerial
Foliar, ground
Soil
Seed
Cotton
Potato
Cotton
Potato
Cucurbit/Lettuce
Tree fruit
Tree fruit/almonds
Nursery
Turf
Forestry
Citrus
Cucurbit
Cucurbit/Lettuce
Grape
Nursery
Forestry
Cotton
Corn
Soybean
Sugarbeet
Wheat
Imidacloprid RQ is higher
Clothianidin RQ is higher
Midge acute
Mayfly acute
Mayfly chronic
Midge chronic

Results of Comparative Analysis based on Raby *et al*. Data: Dinotefuran vs. Imidacloprid



66


Results of Comparative Analysis based on Raby et al. Data: Thiamethoxam vs. Imidacloprid
Foliar, aerial
Foliar, ground
Soil
Seed
100.0
10.0
1.0
0.1
Ratio of Imidacloprid RQ to Thiamethoxam RQ
Imidacloprid RQ is higher
Thiamethoxam RQ is higher
Cotton
Potato
Cucurbit/Lettuce
Nursery
Cotton
Potato
Cucurbit/Lettuce
Tree fruit
Tree fruit/almonds
Nursery
Turf
Forestry
Citrus
Cucurbit
Cucurbit/Lettuce
Radish/carrot
Radish/onion
Grape
Cranberry
Nursery
Turf
Forestry
Cotton
Corn
Soybean
Sugarbeet
Wheat
Midge acute
Mayfly acute
Mayfly chronic
Midge chronic
67

Next Steps and Ongoing Work

- Briefings for AA
- Finalize bee risk assessments
- Complete work on RA supporting attachments (residue bridging strategy, etc.)
- Complete response to comments, addendums, and data reviews

A future step is to synthesize the "lessons learned" from the bridging strategy and the pollen weighting factor and consider implications for risk assessments for other chemicals. this will also include revisiting BeeREX.

Marietta might ask about the mitigations that are being considered. I suggest that you be prepared to summarize the big picture of the mitigation

EFED Neonicotinoid Chemical Teams

Chemical	EFED Branch	Eco	Fate
Clothianidin	ERB 6	Michael Wagman	Chuck Peck
Thiamethoxam (combined document)	ERB 1	Kris Garber Ryan Mroz	Chris Koper
Imidacloprid	ERB 5	Keith Sappington Meghann Niesen Hannah Yingling	Mohammed Ruhman
Dinotefuran	ERB 3	Elizabeth Donovan	Rochelle Bohaty
Coordination and supporting roles		Colleen Rossmeisl Frank Farruggia Monica Wait	